

Attorney Docket No. 49950-59776
U.S.S.N. 09/885,297
Applicants: Ingram *et al.*

Examiner: Rao, Manjunath N.
Group Art Unit: 1652

REMARKS

Claims 44-49, 51-53, 55-59, 97-99, 101, 102, 104, and 105 are pending in the instant application. Claim 44 has been amended and claim 105 has been cancelled. Accordingly, claims 44-49, 51-53, 55-59, 97-99, 101, 102 and 104 will remain pending upon entry of the instant amendment.

Independent claim 44 has been amended to recite that the recombinant host comprises a polynucleotide segment that expresses an additional enzyme. Likewise, page 5 of the specification has been amended to recite that in one embodiment of the recombinant host aspect of the invention, the recombinant host expresses an additional enzyme. Support for the amendment to claim 44 and page 5 of the specification can be found in the claims and specification as originally filed. In particular, support can be found at least, for example, in the specification at page 3, lines 1-27; at page 16, line 22 through page 17, line 2; at page 25, lines 9-20; page 27, lines 14-21; in Example 1, at page 41, line 14 through page 42, line 21; and in Example 4 beginning at page 62 and Table 13. No new matter has been added.

Claim 105 has been cancelled without waiver or prejudice as directed to non-elected subject matter. Amendment and cancellation of the claims is not to be construed as acquiescence to any of the rejections set forth in this Office Action or any previous Office Action, and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the originally filed claims as well as claims directed to non-elected subject matter in further patent applications.

Claim Rejections – 35 U.S.C. §112

Claims 44 and 97-98, claims 45-49, 51-53, 55-59, 99, 101-102 and 104, all of which depend from claims 44 and 97-98 are rejected under 35 U.S.C. §112, second paragraph as indefinite. The Examiner alleges that the phrase "derived from *Erwinia*" is unclear as to its metes and bounds because the term "derived" could be interpreted to mean "to isolate from or obtain from a source", "to arrive at by reasoning i.e., to deduce or infer", or to produce or obtain from another source". The Examiner further alleges because "applicants have not

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provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean, that celZ and celY 'derived from *Erwinia*' encompasses nucleic acid sequences which are recombinants, variants, or mutants encoding any endoglucanase from any source." (Office Action, page 3, top.) The Examiner further indicates that this interpretation has been applied to the claims for all the other rejections made in the Office Action. Applicants respectfully disagree and traverse the rejection.

The Examiner states that Applicants have not provided a definition of "derived from". The Examiner is incorrect. Applicants did indeed provide a definition of that phrase and respectfully invite the Examiner's attention to the instant specification at page 18, lines 24-28, that defines "derived from" as follows:

The term "derived from" is intended to include the isolation (in whole or in part) of a polynucleotide segment from an *indicated source* or the purification of a polypeptide from an *indicated source*. The term is intended to include, for example, direct cloning, PCR amplification, or artificial synthesis from, or based on, a sequence associated with the *indicated polynucleotide source*. (Emphasis added.)

When one of ordinary skill in the art construes the claim 44 recitation "wherein said first endoglucanase is encoded by celZ and said second endoglucanase is encoded by celY, and wherein celZ and celY are derived from *Erwinia*" in light of the foregoing definition, he/she will clearly understand that the recitation encompasses endoglucanases encoded by polynucleotide segments that are isolated in whole or in part from celZ and celY of *Erwinia* (the indicated source). In accordance with the definition, the polynucleotide sequences that encode the endonucleases include those that are obtained by direct cloning, PCR amplification, or artificial synthesis from, or based on, a sequence associated with celZ and celY of *Erwinia*, including recombinants, variants or mutants of celZ and celY of *Erwinia*.

Applicants note that in construing the subject phrase as meaning nucleic acid sequences which are recombinants, variants or mutants encoding *any* endoglucanase from *any* source, the Examiner improperly ignores the claim phraseology "celZ and celY of *Erwinia*", i.e., the "indicated source" recited in the definition. Therefore, in the specific context of the language of claim 44 as presented herein, the Examiner's interpretation of the subject phrase is overly broad.

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Because this overly broad interpretation is the foundation for the remaining rejections of the claims under 35 U.S.C. §112, first paragraph, and 35 U.S.C. §102, those rejections must necessarily fall, as explained more fully below.

Claims 44 and 97-98, claims 45-49, 51-53, 55-59, 99, 101-102 and 104, all of which depend from claims 44 and 97-98 are further rejected under 35 U.S.C. §112, second paragraph as indefinite, because of the recitation "additional enzymes". In particular, the Examiner alleges that it is not clear as to the metes and bounds of that recitation, nor as to whether the additional enzyme is added along with the host cell or whether the additional enzyme is expressed by the host cell. Applicants respectfully disagree and traverse the rejection.

Applicants submit that when one of ordinary skill in the art construes the phrase "additional enzymes" in light of the specification (*see, e.g.*, page 3, lines 1-27), he/she will understand that the additional enzymes contemplated by the invention are any enzymes that enhance expression and secretion of the desired enzymes, *e.g.*, endoglucanases, as well as any enzymes that enhance production of ethanol from organic matter/bagasse. Thus, the specification teaches that such additional enzymes include glucanase, endoglucanase, exoglucanase, cellobiohydrolase, β -glucosidase, endo-1,4- β -xylanase, α -xylosidase, α -glucuronidase, α -L-arabinofuranosidase, acetyl esterase, acetyl xylan esterase, α -amylase, β -amylase, glucoamylase, pullulanase, β -glucanase, hemicellulase, arabinosidase, mannanase, pectin hydrolase, pectate lyase, ethanologenic enzymes (*e.g.*, pyruvate decarboxylase and alcohol dehydrogenase), secretory enzymes (*e.g.*, *pul* and *out* gene products) or a combinations thereof. (*See, e.g.*, the specification at page 4, lines 23-27; and at page 5, lines 33-37.)

Further, without acquiescing to the rejection and in order to expedite prosecution, claim 44 has been amended to recite that the recombinant host comprises a polynucleotide segment that expresses an additional enzyme. Likewise, page 5 of the specification has been amended to recite that in one embodiment of the recombinant host aspect of the invention, the recombinant host expresses an additional enzyme.

Applicants submit that claim 44, when construed by one of ordinary skill in the art in light of the specification, is sufficiently clear and definite, and meets the requirements of 35 U.S.C. §112, second paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under the second paragraph of 35 U.S.C. §112.

Claims 44-49, 51-53, 55-59, 99, 101-102 and 104 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. Specifically, the Examiner alleges that the specification does

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not reasonably provide enablement for claims directed to recombinant host cells suitable for degrading an oligosaccharide comprising any two endoglucanases from any source as the first and second endoglucanases under the control of any surrogate promoter from any source and such recombinant host cell further comprising additional ethanologenic enzymes. Applicants respectfully disagree and traverse the rejection.

Applicants note on page 3, top, of the Office Action, the Examiner acknowledges that he had indicated as allowable a previous claim reciting the phrase "derived from *Erwinia*" and expresses his regret at having missed the phrase. (The previous claim to which the Examiner refers is original dependent claim 54 which the Examiner indicated would be allowable if rewritten as an independent claim and including all the limitations of any intervening claims. Claim 44 as presented herein is such an independent claim.) The Examiner further indicates that his current broad interpretation of the subject phrase is the one he used in considering the claims for all the other rejections. Thus, it would appear that the Examiner takes the position that because of the broad interpretation he ascribes to the subject phrase, the broad claims are not enabled.

However, as noted above, the Examiner's broad interpretation of this phrase, as it appears in claim 44, is incorrect. Applicants submit that based on the correct interpretation of this phrase as set forth above in Applicants' traversal of the Section 112, second paragraph, rejection, the claims are fully enabled by the specification under the first paragraph of Section 112.

The Examiner's attention is invited to working Examples 1-5. These examples set forth detailed teachings on how to make and use the invention commensurate in scope with claim 44. More particularly, Example 1 teaches how to make and use a recombinant *E. coli* host that expresses heterologous *celZ* and *pul* polynucleotides derived from *Erwinia*. Example 2 teaches how to make and use a recombinant *K. oxytoca* host that expresses a heterologous *celZ* polynucleotide derived from *Erwinia*, as well as heterologous *adh* and *pdc* polynucleotides derived from *Z. mobilis* that express additional ethanologenic enzymes, and a heterologous polynucleotide expressing an additional polysaccharase enzyme. Example 3 teaches how to make and use a recombinant *E. coli* host that expresses heterologous *celY* and *celZ* polynucleotides derived from *Erwinia* for the synergistic hydrolysis of carboxymethyl cellulose and acid-swollen cellulose. Example 4 teaches how to make and use a recombinant *K. oxytoca* host that expresses heterologous *celYZ* and *celZ* polynucleotides derived from *Erwinia*, as well as heterologous *adh* and *pdc* polynucleotides derived from *Z. mobilis* that express additional

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ethanologenic enzymes, and a heterologous *out* polynucleotide expressing an additional secretory enzyme to achieve synergistic expression of the endoglucanases. These working examples also detail all the techniques involved for plasmid and vector production, chromosomal integration, identification and isolation of surrogate promoters, and other procedures in accordance with the invention.

Applicants submit that at the time the application was filed, the level of skill in this art was high, and the underlying technology of recombinant organisms expressing heterologous ethanologenic polynucleotides for ethanol production was known and well developed. Based on the correct construction of claim 44, Applicants submit that one of ordinary skill in the art, guided by the working examples provided by Applicants, would be able to practice the invention commensurate in scope with claim 44 without undue burden or experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under the first paragraph of 35 U.S.C. §112.

Claim Rejections – 35 U.S.C. §102

Claims 97-102, 104 and 110 are rejected under 35 U.S.C. §102(b) as being anticipated by W. Liebl, *et al.*, "Analysis of a *Thermotoga maritime* DNA Fragment Encoding Two Similar Thermostable Cellulases, CelA and CelB, and Characterization of the Recombinant Enzymes", *Microbiology*, 142: 2533-2542 (1996) or K. Riedel, *et al.*, Intramolecular Synergism in an Engineered Exo-Endo-1,4- β -Glucanase Fusion Protein", *Molecular Biology*, 28(4): 767-775 (1998). Applicants respectfully disagree and traverse the rejection. (Applicants note that claim 110 was cancelled in Applicants previous Amendment and Response.)

To anticipate a claim, a reference must disclose, either explicitly or inherently, each and every element of the claim. Leibl, *et al.* disclose a recombinant *E. coli* engineered to express two β -glucanases, CelA and CelB, of *Thermotoga maritima*, under control of an efficient host promoter, that are capable of hydrolyzing cellulose. Based on the Examiner's broad interpretation of *celY* or *celZ derived from Erwinia*, to the effect that the phrase encompasses nucleic acid sequences that are recombinants, variants or mutants encoding *any* endoglucanase from *any* source, the Examiner concludes that the CelA and CelB of the reference encompasses the claimed endoglucanases. Applicants disagree.

As noted above, the Examiner's interpretation of the phrase at issue is incorrect. The correct interpretation of that phrase is as set forth in Applicants' argument traversing the Section

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112, second paragraph, rejection of the claims. Based on the correct interpretation, Leibl, *et al.* neither teach nor suggest *celY* or *celZ* derived from *Erwinia*. Accordingly, the reference cannot be said to anticipate the claim.

The Examiner further states that Riedel, *et al.* disclose an identical host cell, *E. coli*, that comprises two endoglucanases CelY and CelZ under the control of surrogate promoter and which are capable of degrading an oligosaccharide/polysaccharide. The Examiner concludes, based on the same incorrect interpretation of "derived from *Erwinia*", that the CelA and CelB of the reference encompasses the claimed endoglucanases. Applicants disagree.

Riedel, *et al.* disclose a recombinant *E. coli* transformed with a fusion of the genes coding for the exoglucanase CelY and the endoglucanase of CelZ from *Clostridium stercorarium*. The recombinant *E. coli* expressed an artificial multienzyme CelYZ that exhibited both exo- and endoglucanase activities. However, based on the correct interpretation of the phrase "derived from *Erwinia*", none of the *Clostridium stercorarium* CelY, CelZ or the CelYZ fusion would be considered "derived from *Erwinia*" as that phrase is used in the pending claims. Thus, Riedel, *et al.* neither teach nor suggest *celY* or *celZ* derived from *Erwinia*. Accordingly, the reference cannot be said to anticipate the claim.

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §102(b) over either the Liebl, *et al.* reference or the Riedel, *et al.* reference.

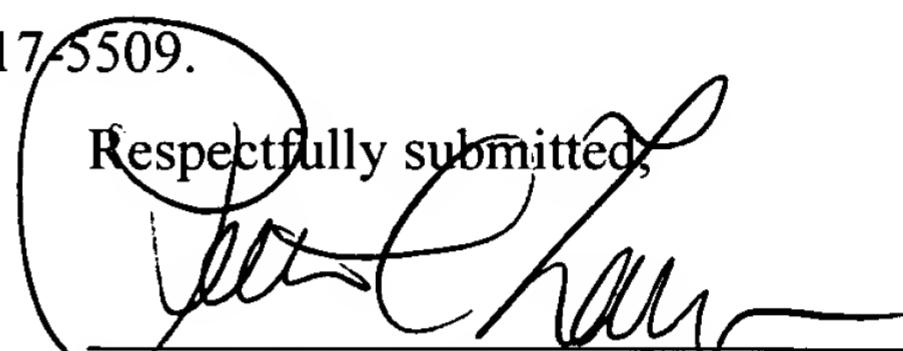
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CONCLUSION

In view of the foregoing amendments and remarks, favorable reconsideration and withdrawal of all rejections, and allowance of this application with claims 44-49, 51-53, 55-59, 97-99, 101, 102 and 104 are respectfully solicited. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 517-5509.

Respectfully submitted,


Peter C. Lauro, Esq.
Registration No. 32,360
Attorney for Applicants

EDWARDS & ANGELL, LLP
P.O. Box 55874
Boston, Massachusetts 02205
Tel. (617) 517-5509
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